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L-Carnitine and CoQ10 Supplementation: Safety Considerations from Real-World Data with Implications for Health and Sport

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Abstract

Background/Objectives: L-carnitine is a naturally occurring compound involved in energy metabolism, while Coenzyme Q10 (CoQ10) is primarily indicated for CoQ10 deficiency and as adjuvant therapy in chronic heart failure. Both are widely used off-label in sports to enhance performance, reduce fatigue, and improve recovery. Despite their popularity, their safety profiles are mainly derived from pre-marketing studies conducted in deficient or clinical populations, not in athletes. Given this limitation, the present study aimed to evaluate and compare the real-world safety profiles of L-carnitine and CoQ10 using spontaneous reports of adverse drug reactions (ADRs) from the EudraVigilance database. **Methods:** EudraVigilance, managed by the European Medicines Agency (EMA), collects spontaneous reports of suspected ADRs related to authorized medicines. ADRs associated with L-carnitine and CoQ10 were analyzed and compared at the System Organ Class (SOC) level using reporting odds ratio (ROR) and proportional reporting ratio (PRR). **Results:** For L-carnitine, the most frequently reported ADRs were gastrointestinal disorders, followed by skin and subcutaneous tissue disorders, general disorders, and nervous system disorders. For CoQ10, the most common ADRs were general disorders and administration site conditions, followed by nervous system disorders, investigations, and gastrointestinal disorders. Comparative analysis (ROR and PRR) showed that CoQ10 was associated with a higher probability of reporting certain ADR categories, particularly blood and lymphatic disorders, musculoskeletal and connective tissue disorders, and nervous system disorders. **Conclusions:** Although L-carnitine and CoQ10 are widely perceived as safe and commonly used by athletes, real-world data highlight the need for increased awareness of potential risks. Continuous monitoring and periodic reassessment of their benefit–risk profile are essential, especially considering their widespread off-label use.

Keywords: L-carnitine; Coenzyme Q10; sports supplementation; supplements safety; individual cases safety reports

1. Introduction

L-carnitine is a quaternary ammonium cation, either synthesized in metabolically active organs such as kidney, liver and brain or can be assimilated through specific foods; the best sousrces are animal products like meat, fish, poultry, and milk [1]. With the involvement of vitamin C, vitamin B6, niacin, and iron, carnitine is primarily synthesized in the body starting from the amino acids lysine and methionine [2]. CoQ10 (CoQ10) is used in sports to boost energy metabolism, reduce

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oxidative stress, and enhance recovery, typically at dosages of 30–300 mg daily [3]. Studies indicate it may improve power output, increase VO2 max, and lower markers of muscle damage like creatine kinase (CK) [4]. The ability of L-carnitine to carry long-chain fatty acids into the mitochondria, the cell's powerhouse where they are oxidized to make energy, is its most well-known property. During times of elevated energy demand, such as exercise or fasting, this process is especially important [5].

L-carnitine is indicated for the treatment of primary and secondary carnitine deficiency and used by athletes. L-carnitine is used in sports primarily to enhance endurance, improve fat metabolism, and speed up recovery by reducing exercise-induced muscle damage and soreness. The use of L-carnitine in sport is considered an off-label use [6]. Frequency of adverse reactions to L-carnitine are reported to be very rare (<1/1000). According to the SOC level they are described in descending frequency order as follows: gastrointestinal disorders (vomiting, nausea, diarrhoea, abdominal cramp), general disorders and administration site conditions (body odour), investigations (International Normalised Ratio increased) (https://www.medicines.org.uk/emc/product/15069/smpc#gref). However, this safety profile is essentially based on pre-registration studies deriving by administration in people with carnitine deficiency.

CoQ10 (ubiquinone or ubidecarenone) is indicated in cases of proven CoQ10 deficiency, as adjuvant therapy to alleviate the symptoms of chronic heart failure as indicated in the summary of product characteristics (https://bpb-eu-w2.wpmucdn.com/blogs.bristol.ac.uk/dist/e/1083/files/2024/06/SmPC-Myoqinon-EN-translation.pdf). CoQ10, has garnered attention for its antioxidant and anti-fatigue properties. It is an endogenous, lipophilic, vitamin-like molecule, involved into the mitochondrial respiratory chain, furthere it works as an electron carrier [7,8]. After administration, in the blood, the oxidized form ubiquinone is reduced to the antioxidant ubiquinol. CoQ10 has protective function against peroxidation of phospholipids, mitochondrial membrane proteins, and deoxyribonucleic acid (DNA) [9]. It is used in athletes to enhance energy metabolism (ATP production), reduce exercise-induced oxidative stress, and improve recovery [10]. Also the administration of CoQ10 in sport is generally considered an off-label use. Undesirable effects reported in the summary of product characteristics, associated with its approval, include gastrointestinal symptoms, headache, dizziness and cutaneous reactions. According to the system organ class (SOC) level they are described in the summary of product characteristics, in descending frequency order, as follows: nervous system disorders (headache, dizziness), gastrointestinal disorders (nausea, constipation, diarrhoea, pain in the stomach area, indgestion), skin and subcutaneous tissue disorders (rash, itching). As happens for L-carnitine the known safety profile is based on pre-marketed studies not conducted on sport activity.

These two substances share aspects regarding the off label use in sport activity and the common perspective regarding their known safety profile, essentially based on pre-registration studies conducted on patients who needed a treatment due to deficiency of L-carnitine or CoQ10. Consequently, we decided to investigate on safety profile of the two substances and to compare the results obtained as it is revealed by real-world data, through the analysis of spontanepus reports of adverse reactions of the datasystem EudraVigilance.

2. Methods

EudraVigilance is a database containing suspected adverse reactions (SARs) related to medicines authorized for the market or currently undergoing clinical trials. In this data system, SARs are traceable in individual cases (Individual Cases Safety Reports; ICSRs) signaled by national drug regulatory authorities in the European Union (EU) or by marketing authorization holders. EudraVigilance collects reports of "suspected" adverse reactions, meaning unwanted medical events that have been observed following the use of a medicine, but which are not necessarily related to or caused by the medicine itself [11].

In this study, ICSRs reporting SARs that occurred in patients taking carnitine or CoQ10, signaled until 31 december 2025, were collected and analyzed. The public version of the EudraVigilance

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database was used and collection of data on SARs was conducted according to the following inclusion criteria: serious and not-serious SARs, cases regarding all the ages (from 0 to > 85 years) and both the sexes. For all cases, information was provided on patient characteristics (age and sex), type of adverse reaction (often more than one for each ICSR), qualification of the primary source. The terms "sex" and "gender" are used interchangeably here because only the field containing the term "sex" is available in EudraVigilance, consequently the information collected refers to biological sex [12]. Regarding the data selection criteria, in ICSRs, SARs selection was based on the Medical Dictionary for Regulatory Activities (MedDRA). MedDRA is an international standardized and clinically validated medical terminology used by regulatory authorities and the biopharmaceutical industry. It is used to code cases of adverse effects in pharmacovigilance databases and to facilitate searches in the databases on adverse drug reactions. For the present study, each ICSR was analyzed and every mentioned SAR was extracted and counted from every single case. Single adverse reactions were described using the so-called "Preferred terms" (PTs) listed in MedDRA. A PT is a distinct descriptor (single medical concept) for an adverse symptom or sign. We selected all the PTs that were recorded in each ICSR, we counted them all and analyzed the frequencies for every adverse reaction. Two or more PTs with overlapping clinical meaning were aggregated to avoid unnecessary duplicate PTs with the same connotation. MedDRA has a hierarchy of terms to describe adverse reactions. Adverse reactions were also grouped under the terms of the SOC (System Organ Class) level in the MedDRA hierarchy such as for example "Musculoskeletal and connective tissue disorders", "Vascular disorders", etc. Each single PT has been associated to the corresponding SOC level by using the MedDRA terminology reported by the National Center for Biomedical Ontology (NCBO). The SOC system organ classification is the highest level of the hierarchy that captures the broadest concept useful for retrieving data. It is a way of grouping medical terms based on body systems or functions [13]. A disproportionality analysis of adverse reactions aggregated according to the SOC level was performed by calculation of reporting odds ratio (ROR) and proportional reporting ratio (PRR) comparing data of signals of spontaneous reports related to the intake of L-carnitine and CoQ10. The Reporting Odds Ratio (ROR) is a disproportionality measure used to identify safety signals through the comparison the odds of a specific adverse event signaled to be linked to the use of a particular drug versus the odds of the same adverse event signaled with other drugs [14].

The PRR is a disproportionality measure useful to identify if a drug-event combination is reported at a higher-than-expected rate relative to other products [15].

As source of data extraction, a line listing structured table where each row represents an ICSR, and each column represents a specific data point associated with that case. Data were analyzed by aggregating the PTs of individual reports to a higher level of the MedDRA hierarchy by merging individual SARs in the SOC level (e.g., nausea and vomiting classified in the same group as Gastrointestinal Symptoms). Adequate stratification of signals by sex groups was performed to avoid biases caused by confounding effects and to analyze this variable separately. Duplicate ICSRs were excluded from the analysis. Duplicate search was based on detection in the dataset of similarities in adverse reaction, age, sex, suspected/interacting medicinal products, EudraVigilance local report number. A descriptive statistical analysis was performed by using SPSS statistical software, version 29.0 (SPSS, IBM, Armonk, NY, USA).

3. Results

ICSRs reporting suspected adverse reactions to L-carnitine in EudraVigilance were 257. Serious/non serious cases ratio for L-carnitine was 0.52 and percentage of serious cases 34.2% of the total number of signals. ICSRs reporting suspected adverse reactions to CoQ10 found in EudraVigilance were 271. Serious/non serious cases ratio to CoQ10 was 2.93 and percentage of serious cases 74.5% of the total number of signals of adverse reactions to ubidecarenone (Table 1).

Individual cases with SARs to L-carnitine were distributed according to their age as follows: 0-1 month (3), 1.2%, 2 months–2 years (8) 3.1%, 3–11 years (9) 3.5%, 12–17 years (9) 3.5%, 18–64 years (120) 46.7%, 65–85 years (62) 24.1%, more than 85 years (5) 1.19% and not specified (41) 15.9% (Figure

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1). Sex distribution showed the apparent prevalence of signals of adverse reactions occurring in females (61.5%). Most frequently signaled adverse reactions, according to the analysis of the frequency of PTs, were in decreasing order: dizziness/vertigo, abdominal discomfort/abdominal pain, urticaria/pruritus, nausea, erythema, agitation, diarrhoea, paraesthesia, vomiting, tremor. However, statistically significant differences of female prevalence was showed only for the adverse reaction "agitation" (Table 2).

ICSRs with SARs to CoQ10 were distributed according to their age as follows: 0-1 month (1), 0.4%, 2 months–2 years (5) 1.8%, 3–11 years (7) 2.6%, 12–17 years (5) 1.8%, 18–64 years (105) 38.7%, 65–85 years (94) 34.7%, more than 85 years (9) 3.3% and not specified (44) 16.2% (Figure 1). Sex distribution showed the prevalence of signals of adverse reactions occurring in females (61.6%). Most frequently signaled adverse reactions to CoQ10, according to the analysis of the frequency of PTs, were in decreasing order: abdominal discomfort/abdominal pain, nausea, arthralgia/arthritis, rash, acute hepatic failure/hepatitis, anaemia, blood pressure decreased. Analysis of sex distribution of the single adverse reactions to L-carnitine showed an apparent prevalence of signals regarding females (61.6%) over males (Table 2). No significant difference was shown in sex distribution of single adverse reactions to CoQ10 (Table 3).

After aggregation of the adverse reactions according to the SOC level the results of the disproportionality test, calculated as ROR and PRR, show as the use of L-carnitine produced spontaneous reports of adverse reactions regarding gastrointestinal disorders (14.6%), skin and subcutaneous tissue disorders (14.0%), general disorders and administration site conditions (13.75%), nervous system disorders (12.44%). Groups of most frequent adverse reactions to CoQ10 were general disorders and administration site conditions (13.07%), nervous system disorders (12.83%), investigations (9.59%), gastrointestinal disorders (9.46%) (Table 4). In Table 4 are also represented the results of the disproportionality test, calculated as ROR and PRR, based on the comparison of CoQ10 and L-carnitine, show that use of CoQ10 is linked to an increase of the probability that blood and lymphatic disorders, musculoskeletal and connective tissue disorders and nervous system disorders could be signaled more frequently in comparison of use of L-carnitine (Table 4).

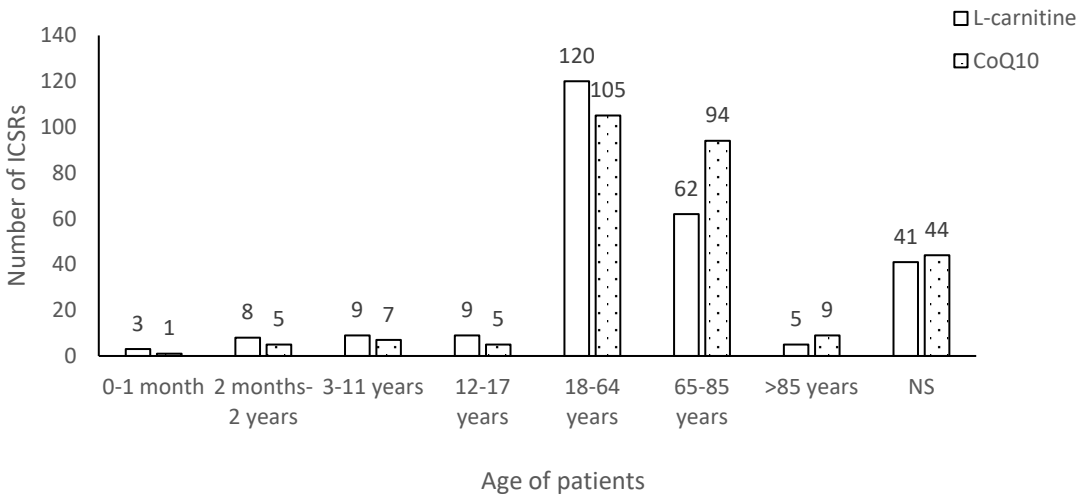

Figure 1. Individual Cases Safety Reports (ICSRs) reporting suspected adverse reactions to L-carnitine and CoQ10, stratified by patient age.

 doi:10.20944/preprints202605.0456.v1

Table 1. Serious/non-serious ratio of Individual Cases Safety Reports (ICSRs) related to L-carnitine and CoQ10 signaled in the European Economic Area and United Kingdom.

Drug	ICSRs (total)	Serious ICSRs	Non-serious ICSRs	ICSRs serious/non-serious ratio
CoQ10	271	202	69	2.93
L-Carnitine	257	88	169	0.52

Table 2. Frequency and sex distribution of cases of suspected adverse reactions (SARs) to L-carnitine in the European Economic Area and the United Kingdom.

SARs	Females Cases = 158	Males Cases = 99	Total cases	Chi square statistic	P value
Dizziness/Vertigo	17	9	26	0.1864	0.665969
Abdominal discomfort/ Abdominal pain	19	5	24	3.4972	0.061472
Urticaria/Pruritus	12	8	20	0.0200	0.887478
Nausea	13	5	18	0.9434	0.331412
Erythema	8	4	12	0.1431	0.705253
Agitation	10	1	11	4.2030	0.040352*
Diarrhoea	4	7	11	3.0608	0.080204
Paraesthesia	8	3	11	0.6140	0.433286
Vomiting	8	2	10	1.5072	0.219574
Tremor	5	5	10	0.5789	0.446752
Rash	5	4	9	0.1382	0.710115
Headache	7	1	8	2.3608	0.124418
Insomnia	6	2	8	0.6374	0.424638
Tachycardia/Palpitations	4	4	8	0.4594	0.497912
Dyspepsia	4	3	7	0.0571	0.811106
Hypertension	3	3	6	0.3418	0.558796
Confusional state	2	3	5	0.9933	0.318933
Dyspnoea	4	1	5	0.7386	0.390102
Hallucination	4	1	5	0.7386	0.390102

Only adverse reactions signaled more than four times are reported. * = $P < 0.05$.

Table 3. Frequency and sex distribution of cases of suspected adverse reactions (SARs) to CoQ10 in the European Economic Area and the United Kingdom.

SARs	Females Cases = 167	Males Cases = 104	Total cases	Chi square statistic	P value
Abdominal discomfort/ Abdominal pain	24	9	33	1.959	0.161624
Nausea	3	4	7	0.9434	0.331412
Arthralgia/arthritis	6	1	7	1.0701	0.300927
Rash	2	4	6	2.0765	0.149580
Acute hepatic failure/Hepatitis	2	3	5	1.0072	0.315582
Anaemia	2	3	5	1.0072	0.315582
Blood pressure decreased	2	3	5	1.0072	0.315582

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Only adverse reactions signaled more than four times are reported.

Table 4. Reporting odds ratio (ROR) and proportional reporting ratio (PRR) of suspect adverse reactions (SARs) of CoQ10 versus Carnitine aggregated according to the System Organ Class (SOC) level.

SOC	SARs to CoQ10 N. and (%)	All other SARs to CoQ10	SARs to Carnitine N. and (%)	All other SARs to carnitine	ROR carnitine vs ubichinone (95% C.I.)
Blood and lymphatic system disorders	21 (2.61%)	782	4 (0.87%)	454	**ROR: 3.04 PRR: 2.99 (1.04-8.93)**
Cardiac disorders	30 (3.73%)	773	18 (3.93%)	440	ROR: 0.69 PRR: 0.70 (0.39-1.22)
Ear and labyrinth disorders	14 (1.74%)	789	9 (1.96%)	449	ROR: 0.88 PRR: 0.89 (0.38-2.06)
Eye disorders	21 (2.61%)	782	9 (1.96%)	449	ROR: 1.34 PRR: 1.33 (0.61-2.95)
Gastrointestinal disorders	76 (9.46%)	727	67 (14.6%)	391	ROR: 0.61 PRR: 0.65 (0.43-0.87)
General disorders and administration site conditions	105 (13.07%)	698	63 (13.75%)	395	ROR: 0.94 PRR: 0.95 (0.67-1.32)
Immune system disorders	11 (1.37%)	792	7 (1.53%)	451	ROR: 0.89 PRR: 0.90 (0.34-2.32)
Infections and infestations	35 (4.36%)	768	10 (2.18%)	448	ROR: 2.04 PRR: 2.00 (1.00-4.16)
Injury, poisoning and procedural complications	53 (6.60%)	750	29 (6.33%)	429	ROR: 1.04 PRR: 1.04 (0.65-1.67)
Investigations	77 (9.59%)	726	21 (4.58%)	437	**ROR: 2.21 PRR: 2.09 (1.34-3.63)**
Metabolism and nutrition disorders	25 (3.11%)	778	16 (3.49%)	442	ROR: 0.89 PRR: 0.89 (0.47-1.67)
Musculoskeletal and connective tissue disorders	53 (6.60%)	750	12 (2.62%)	446	**ROR: 2.63 PRR: 2.52 (1.34-4.97)**
Nervous system disorders	103 (12.83%)	700	57 (12.44%)	401	**ROR: 5.47 PRR: 4.89 (2.97-10.06)**
Psychiatric disorders	41 (5.10%)	762	34 (7.42%)	424	ROR: 0.67 PRR: 0.69 (0.42-1.07)
Renal and urinary disorders	14 (1.74%)	789	14 (3.06%)	444	ROR: 0.56 PRR: 0.57

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					(0.26-1.19)
Reproductive system and breast disorders	13 (1.62%)	790	3 (0.65%)	455	ROR: 2.49 PRR: 2.47 (0.71-8,80)
Respiratory, thoracic and mediastinal disorders	31 (3.86%)	772	15 (3.27%)	443	ROR: 1.18 PRR: 1.18 (0.63-2.22)
Skin and subcutaneous tissue disorders	54 (6.72%)	749	64 (14.00%)	394	ROR: 0.44 PRR: 0.48 (0.30-0.65)
Vascular disorders	26 (3.24%)	777	9 (1.96%)	449	ROR: 1.67 PRR: 1.65 (0.77-3.59)

C.I. = confidence intervals.

4. Discussion

L-carnitine is crucial for the transport of long-chain fatty acids into the mitochondria, where they are oxidized to produce ATP, the primary energy currency of cells. During periods of endurance exercise or prolonged physical activity, the body typically relies more on fat oxidation to meet energy demands, especially once glycogen stores become depleted. During exercise, through the increase of the availability of fatty acids for mitochondrial oxidation, L-carnitine supplementation may improve fat metabolism and increases the use of fat as a primary fuel source rather than carbohydrate. Thus, allowing athletes to maintain energy levels for a longer period while sparing glycogen stores [16].

Several authors showed the beneficial effects of CoQ_{10} supplementation in health and disease conditions. Furthermore, it has been shown that the increase in plasma concentration of CoQ_{10} after its intake, promotes enhancement of performance indicators and better recovery in athletes [4,10]. Some studies have reported positive effects of intake of CoQ10 on physical performance and exercise-induced muscle damage. While some findings showed as CoQ10 intake supplementation alleviates the muscle damage caused by exercise and increases physical performance, other authors report insufficient proof of these effects [9].

Anyway, both these drugs are frequently used by athletes and non athletes with public knowledge of safety essentially based on pre-registration studies used for medicinal products containing them.

About the safety of L-carnitine intake, results of a study investigating on toxic effects of 8-week oral supplementation of l-carnitine (0.3 and 0.6 g/kg) in female and male rats, showed that L-carnitine reduced body and fat weights, as well as serum, liver, and kidney lipid levels. Simultaneously, hepatic fatty acid β-oxidation and lipid synthesis were disturbed. Moreover, L-carnitine accelerated reactive oxygen species production in serum and liver, thereby triggering hepatic NOD-like receptor 3 (NLRP3) inflammasome activation to elevate serum interleukin (IL)-1β and IL-18 levels. Alteration of serum alkaline phosphatase levels further confirmed liver dysfunction in L-carnitine-fed rats. These observations suggested caution for the safety of long-term L-carnitine supplementation [17].

Regarding L-carnitine safety in humans, most studies report good overall tolerability for this substamce. Adverse reactions are usually gastrointestinal disorders, while rarely seizures, metabolic and renal disorders are signaled. It has been reported the case of a patient with riboflavin-responsive mild multiple acyl-CoA dehydrogenation deficiency of the ethylmalonic--adipic aciduria type experiencing several spontaneous hypoglycaemic episodes after supplementation with L-carnitine. Clinical signs were explained in terms of the known biochemical features of this disease but suggested caution in the carnitine supplementation of patients with defective oxidation of medium- or short-chain fatty acyl-CoA esters [18]. A case of fish odor syndrome occurred with L-carnitine supplementation, resolved after withdrawn of the substance, has been reported. This event was associated with excessive carnitine intake and consequent saturation of elimination pathway or

 doi:10.20944/preprints202605.0456.v1

deficiency of enzymatic metabolism [19]. Gastrointestinal adverse reactions such as abdominal cramps and vomiting were reported after treatment with L-carnitine for 12 months in children 0-12 months old. On this basis, supplementaion with L-carnitine was considered justified and appropriate only in 18% of patients [20]. A more recent review, including studies on healthy human subjects treated for at least 12 weeks with oral administration of L-carnitine, with no drugs or any other multi-ingredient supplements co-ingestion, reported that prolonged supplementation may affect physical performance. In the same review, was cited that database of the European Medicine Agency (EudraVigilance) for adverse reactions linked to L-carnitine intake analyzed in a descriptive way the presence of 143 cases, among these, a few reports of tachyarrhythmias and palpitation were found. On the other hand, results of the review reported that L-carnitine supplementation elevates fasting plasma levels of trimethylamine-N-oxide, a substance supposed to be pro-atherogenic. The same authors sustained that additional studies focusing on long-term supplementation and its longitudinal effect on the cardiovascular system are needed [21].

The safety profile of high doses of CoQ10 given for four weeks to 88 healthy persons was established in a double-blind, randomized, placebo-controlled study. During the period of suplementation, no serious adverse events were reported both in verum and placebo group. Common adverse events included cold and gastrointestinal disorders, such as abdominal pain and soft feces, but were not associated with CoQ10 intake [22]. A systematic review, published in 2006, even though accused that the lack of sufficient data necessary to establish a robust risk assessment, indicated a strong evidence of safety of intake normally used for CoQ10, cobsidered a substance with low toxicity at intakes lower that 1200mg/day [23]. Another review, described the safety profile of CoQ10 on the basis of animal and human data. Results indicated that CoQ10 has low toxicity and does not induce serious adverse effects in humans, suggesting that it is highly safe for use [24].

Another recent systematic review conducted by investigating on several databases (Ebsco Host, PubMed, Scopus, Google Scholar) and aiming to evaluate effects of CoQ10 used to improve the symptom fatigue in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome, reported that CoQ10 has a high interaction risk with warfarin and other anticoagulants and that the interaction due to the concomitant intake with Omega-3 fish oil may potentially to the cause of hypotension due to their synergistic antihypertensive effects [25].

In summary, L-carnitine supplementation is generally considered safe and well-tolerated with common adverse reactions represented by gastrointestinal disorders (such as nausea, vomiting, abdominal cramps, and diarrhea), fishy odour in urine, sweat, and breath (due to metabolism of unabsorbed L-carnitine by gut bacteria), headache and fatigue [26]. Also the safety profile of CoQ10 is recognized as favorable, with mostly minor, reversible side effects, but caution is recommended when taken together with anticoagulant drugs (reduction of effects on blood coagulation) [23,24].

Safety profile emerging from results of the present study only partially confirm the shared general view regarding the two conpounds. Serious/non serious cases ratio to CoQ10 was 2.93, higher than the same ratio for L-carnitine. In pharmacovigilance, a higher serious/non-serious cases ratio refers to a greater proportion of reported adverse events that are classified as “serious” relative to those considered non-serious. A higher serious/non-serious ratio may reflect true severity but it is not a risk measure and requires deeper evaluation [27,28]. Most of suspected adverse reactions for L-carnitine were signaled in adults (46.7%) and elders (25.9%). The adverse reaction dizziness/vertigo, reported for L-carnitine, is not normally signaled in its known safety profile, while is the more frequent signal reported in the database EudraVigilance, followed by the adverse reaction abdominal discomfort/abdominal pain. About the sex distribution of suspected adverse reactions, while for CoQ10 no difference has been found between the sexes, a significant difference in the occurrence of the PT agitation was observed in females taking L-carnitine in comparison to males. Most of suspected adverse reactions for CoQ10 were signaled in a similar way in adults (38.7%) and elders (38.0%). The adverse reaction abdominal discomfort/abdominal pain is the more frequent signal reported in the database EudraVigilance for CoQ10, followed by abdominal discomfort/abdominal

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pain. About the sex distribution of suspected adverse reactions, no significant difference was shown in sex distribution of single adverse reactions to CoQ10.

Grouping the adverse reactions according to the SOC level showed that gastrointestinal disorders, followed by skin and subcutaneous tissue disorders, general disorders and administration site conditions, nervous system disorders, are more reported for L-carnitine. Groups of most frequent adverse reactions to CoQ10 were general disorders and administration site conditions, followed by nervous system disorders, investigations, gastrointestinal disorders. Comparison of adverse reactions of the two compounds according to the SOC level and calculated as ROR and PRR, shows that use of CoQ10 is linked to an increase of the probability that some of the categories of disorders are more signaled with use of CoQ10. In particular, blood and lymphatic disorders, musculoskeletal and connective tissue disorders and nervous system disorders.

The picture emerging from the comparison of CoQ10 and L-carnitine shows as these substances, both very common ingredients in dietary supplements [10,29,30], often used in off label prescription or simply advised for professional or not professional athletes have a safety profile not corresponding to that commonly known one. The analysis of real-world data derived from spontaneous adverse drug reaction reports in the EudraVigilance database suggests that the safety profiles of L-carnitine and coenzyme Q10 (CoQ10), generally considered safe and well tolerated, do not fully align with the evidence reported in pre-authorization clinical studies. Furthermore, the disproportionality analysis comparing the signals of adverse reactions of the two medicinal products indicates a relatively less favorable safety profile for CoQ10. In particular, CoQ10 appears to be associated with a higher reporting frequency of adverse events within specific system organ classes, including blood and lymphatic disorders, musculoskeletal and connective tissue disorders, and nervous system disorders.

Overall, these results underscore the critical role of post-marketing pharmacovigilance and real-world evidence in refining the understanding of drug safety. They also emphasize the need for increased awareness among healthcare professionals regarding the potential risks associated with products often used beyond the indications and that are widely perceived as safe. Continuous monitoring and periodic re-evaluation of the benefit–risk balance of L-carnitine and CoQ10 are therefore warranted to ensure their safe use in clinical practice.

Given their widespread use in athletes, these findings highlight the need for careful evaluation of their safety in sport and exercise settings.

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Data Availability Statement: The data analyzed and presented in this study are available on the public EudraVigilance database, https://www.ema.europa.eu/en/human-regulatory-overview/ research-development/pharmacovigilance-research-development/eudravigilance (accessed on 31 december 2025).

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